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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LUKTON, DAVID	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/344,676	Applicant(s) Van Antwerp
	Examiner David Lukton	Art Unit 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 11, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-9, 11-14, 17, 19-23, 25-52, 54, 58-68, and 71* is/are pending in the application.

4a) Of the above, claim(s) *8, 17, 26-52, 54, 58, and 64* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7, 9, 11-14, 19-23, 25, 59-63, 65-68, and 71* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Pursuant to the directives of paper No. 18 (filed 12/11/02), claims 1, 7, 12, 17, 19-21, 33, 35-37, 41, 46, 48-51, 58, 59, 66, 71 have been amended, and claims 10, 15, 16, 18, 24, 53, 55-57, 69, 70 cancelled. Claims 1-9, 11-14, 17, 19-23, 25-52, 54, 58-68, 71 are pending. Claim 19 is now rejoined with the elected claims.

Claims 1-7, 9, 11-14, 19-23, 25, 59-63, 65-68, 71 are examined in part.

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Claims 1-7, 9-14, 19-23, 25, 59-63, 65-68, 71 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 1 is indefinite as to the intended analogs. Applicants have argued that if one looks through the specification, one can attain some insight into what may be intended. Whatever the merits of this assertion, the claims do not state that which applicants have argued is intended. In the event that the claims are amended to recite the limitations that applicants argue are implied, the claims which recite those limitations will be assessed for compliance with §112, second paragraph.

- Claim 1 is rendered indefinite by the recitation of "insulin related peptide". In what way must the peptide in question be "related" to insulin? Applicants have argued that if one looks through the specification, one can attain some insight into what may be intended. Whatever the merits of this assertion, the claims do not state that which applicants have argued is intended. In the event that the claims are amended to recite the limitations that applicants argue are implied, the claims which recite those limitations will be assessed for compliance with §112, second paragraph.

- Claim 19 implies that a liquid is present, since it recites concentration ranges in units of mg/mL. However, claim 1, upon which claim 19 depends, makes no mention of a liquid. One option would be to cast claim 19 in independent form. Another

option would be to amend claim 1 to convey that a liquid is optionally present.

- Claim 19 implies that the claimed composition contains only agent ii and agent iii. However, claim 1 requires agent i to be present as well. One option would be to recite (in claim 19) simply that the concentration of agent (ii) is in the range of 0.05-12.5 mg/mL, and that the concentration of agent (iii) is also in the range of 0.05-12.5 mg/mL.

- Claim 66 implies that a liquid is present, since it recites concentration ranges in units of mg/mL. However, claim 59, upon which claim 66 depends, makes no mention of a liquid. One option would be to cast claim 66 in independent form. Another option would be to amend claim 59 to convey that a liquid is optionally present.

- In claim 61, the phrase "small molecule insulin mimetic material" lacks antecedent basis.

- In claim 61, the term "L-783281" may be used if accompanied by the chemical name that this term represents.

- It is not clear how one should reconcile the mandates of claim 71 with those of claim 59. Given the claim dependence, it is assumed that what is intended for claim 71 is that all three agents (agent i, ii, and iii) must be present, but that in addition to this, at least one additional compound that falls within the scope of agent i, ii, and iii must be present as well, for a total of four separate compounds. If this is the intention, claim 59 should be amended to make this clear. The same issue applies in the case of claim 20 versus claim 1.

- Claim 23 recites "further comprising". This is a limitation which is not required by claim 21, upon which claim 23 depends. This ground of rejection could be overcome by casting claim 23 in independent form. An alternative to this would be to amend claim 21 to recite that the carrier is optionally present.

*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over Rieveley (USP 6,153,632).

As indicated previously, Riveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer.

With respect to claim 1, an "insulin-related peptide" or an "insulin-related peptide analog" could be viewed as encompassing insulin itself. According to one interpretation, insulin could even be regarded as the epitome of an "insulin-related peptide" or an "insulin-related peptide analog". Thus, insulin itself is fulfilling the roles of agents (i) and (ii). A similar argument applies in the case of claim 59. As for claim 71, one of ordinary skill would have been motivated to use two different insulin sensitizers for additive effects.

Thus, the claims are rendered obvious.

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Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over Knudsen (USP 6,268,343) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

As indicated previously, Knudsen discloses (e.g., col 168, line 1-17; also claim 36) a composition comprising insulin and GLP-1. Knudsen does not disclose the use of insulin sensitizers. However, each of Smith and Rieveley disclose the use of insulin sensitizers. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references.

Thus, the claims are rendered obvious.

Although applicants have not had an opportunity to comment on this ground of rejection, applicants have preemptively argued (paper No. 18, filed 12/11/02) that in asserting that a ternary mixture is obvious, there must be a single reference which teaches a composition that contains all three components. However, this is not true; this assertion is nearly equivalent to saying that if a prior art rejection is not imposed under 35 USC §102, it is generally invalid. It is agreed that this rejection is imposed under §103, rather than §102. It is not being argued by the examiner (in this, and some of the other grounds of rejection) that a single reference teaches all three requisite components. But the question is really of motivation to combine compounds. If reference "A"

discloses that two of the compounds recited in instant claim 1 are useful to treat diabetes, for example, and reference "B" discloses that the third compound recited in instant claim 1 is useful to treat diabetes, then one would expect, in advance of experimentation, that the three compounds together would provide an additive effect. In reality, this is not always true. In some cases, the beneficial effect can be less than additive. In rare cases, there can even be an adverse reaction. In other cases, there is a synergistic effect. It may be the case that using a higher dose of A +B provides an effect which is equivalent to using the ternary mixture (A +B + C), but to the extent that this is true, it does not undermine the examiner's position with regard to obviousness. The point is that an obviousness rejection in a situation like this can be entirely proper even if there is no single reference that teaches a composition which contains all three components. The prima facia case for obviousness is on firm ground if there is motivation to combine compounds, which is the case here. If applicants can provide evidence of "unexpected results", such as a synergistic response in rats, then that may be sufficient to overcome the *prima facia* case, at least for certain embodiments within the claimed genus. In the absence of such, however, the rejection is justified. Applicants have also argued that one of the references discloses using an agent in addition to those that are listed in the instant claims. However, if this is true, it does not constitute evidence of non-obviousness. If a claim is drawn to a composition that **comprises** A +B + C, and a

single reference, or combination of references discloses a composition that comprises A +B + C + D, the fact that "D" may also be present does not negate the validity of the rejection, since the instant claims encompass the possibility of having three active agents, or four active agents, or 97 active agents.

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Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over Tomas (WO 96/02270) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

As indicated previously, Tomas discloses a composition comprising insulin and IGF-1. Tomas does not disclose the use of insulin sensitizers. However, each of Smith and Rieveley disclose the use of insulin sensitizers. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references.

Thus, the claims are rendered obvious.

*

Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over Rink (WO 92/20366) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

As indicated previously, Rink discloses a composition comprising insulin and amylin.

Rink does not disclose the use of insulin sensitizers. However, each of Smith and Rieveley disclose the use of insulin sensitizers. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references.

Thus, the claims are rendered obvious.

*

Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over Clark (USP 5,783,556) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

As indicated previously, Clark discloses a composition comprising insulin and IGF-1. Clark does not disclose the use of insulin sensitizers. However, each of Smith and Rieveley disclose the use of insulin sensitizers. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references.

Thus, the claims are rendered obvious.

*

Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over Cooper (USP 5,641,744) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

As indicated previously, Cooper discloses (e.g., col 3, line 37+) a composition comprising insulin and amylin. Cooper does not disclose the use of insulin sensitizers. However, each of Smith and Rieveley disclose the use of insulin sensitizers. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references.

Thus, the claims are rendered obvious.

*

Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over Froesch (USP 4,988,675) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

As indicated previously, Froesch discloses a composition comprising insulin and IGF-1. Froesch does not disclose the use of insulin sensitizers. However, each of Smith and Rieveley disclose the use of insulin sensitizers. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references. Thus, the claims are rendered obvious.

*

Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over Chance (USP 4652548) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

As indicated previously, Chance discloses a composition comprising insulin and C-peptide. Chance does not disclose the use of insulin sensitizers. However, each of Smith and Rieveley disclose the use of insulin sensitizers. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references. Thus, the claims are rendered obvious.

*

Claims 1, 59 and 71 rejected under 35 U.S.C. §103 as being unpatentable over L'Italien (USP 6,136,784) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

As indicated previously, L'Italien discloses (e.g., claim 1) a composition comprising insulin and amylin. L'Italien does not disclose the use of insulin sensitizers. However, each of Smith and Rieveley disclose the use of insulin sensitizers. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references. Thus, the claims are rendered obvious.

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Claims 1, 59 and 71 are rejected under 35 U.S.C. §103 as being unpatentable over Habener (USP 5,958,909) in view of either (a) Smith (WO 98/57636) or (b) Rieveley (USP 6,153,632).

Habener discloses that GLP-1 is useful for treating diabetes. Habener does not disclose combining GLP-1 with insulin and an insulin sensitizer. However, each of Smith and Rieveley disclose the use of insulin in combination with an insulin sensitizer. Thus, one of ordinary skill would have been motivated to use the insulin sensitizers to achieve the advantages disclosed in the secondary references. Thus, the claims are rendered obvious.

✺

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600